

Figure 1

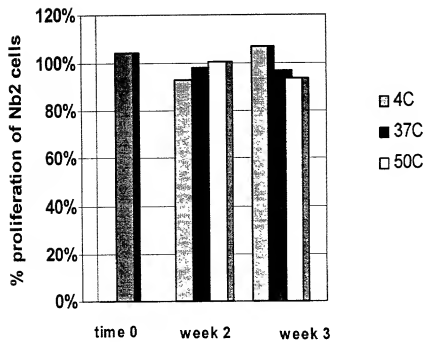


Figure 2

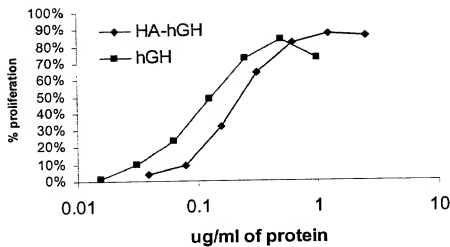


Figure 3A

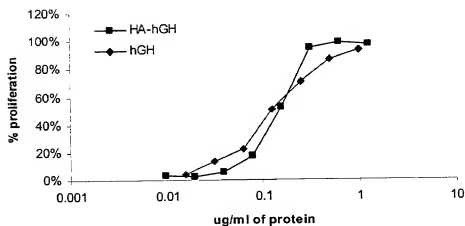


Figure 3B

09833411.002701

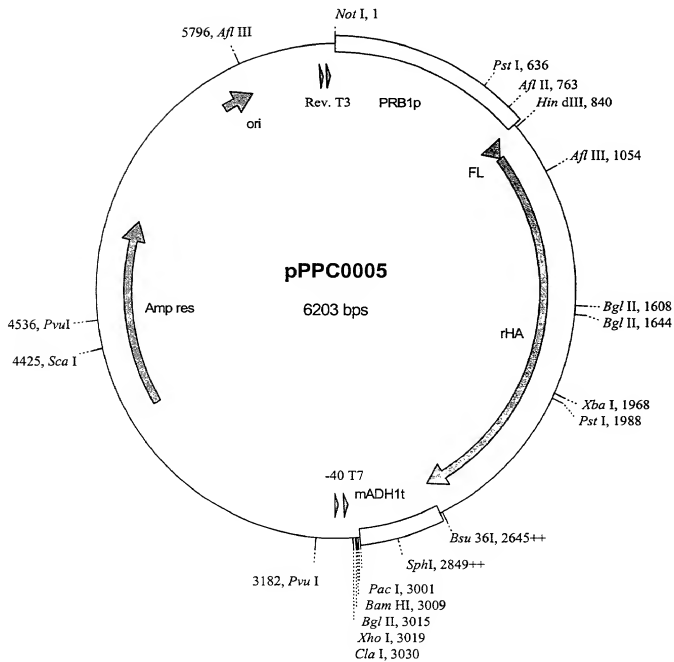


Figure 4

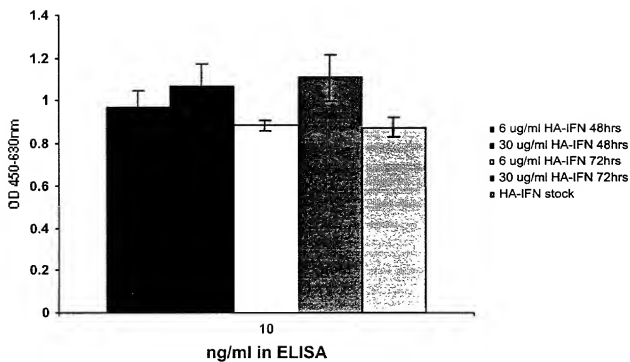
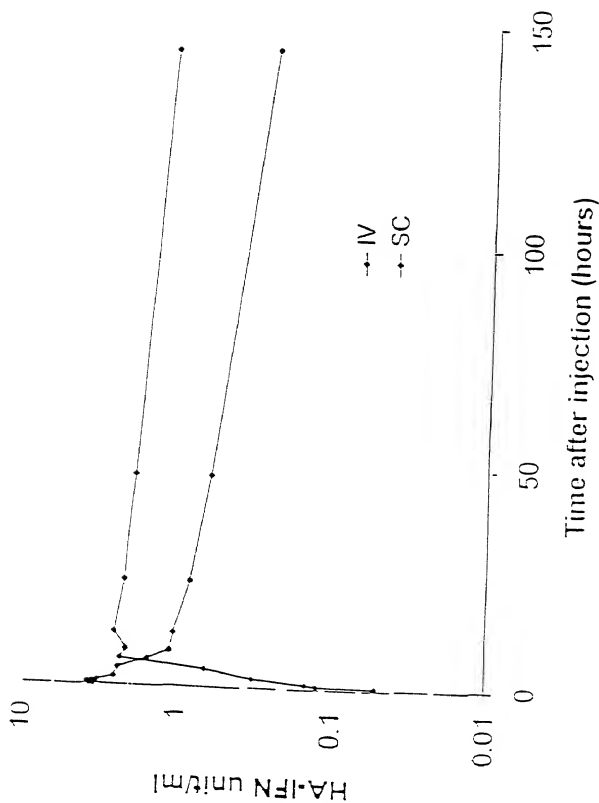


Figure 5

Figure 6



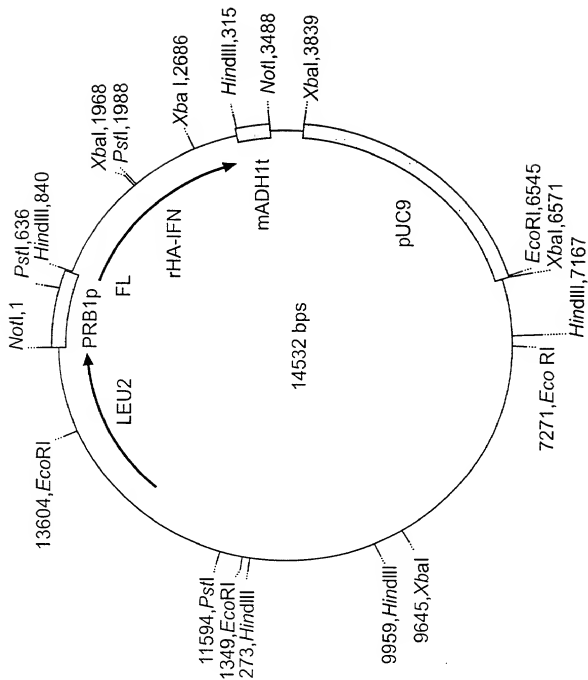


FIG. 8

Figure 9

1 DAHKSEVAHR FKDLGEENFK ALVLIAFAQY LQQCPFEDHV KLVNEVTEFA
 HHHHHH HHH HHH HHHHHHHHHHHH HHHHH HHHHHHHHHHHH

51 I II III
KTCVADESAE NCDKSLHTLF GDKLCTVATL RETYGEMADC CAKOEPERNE
HHHHH HHHHH HHHHH HHHH H HHHHH

101 CFLQHKDDNP NLPRLVRPEV DVMCTAFHDN EETFLKKYLY EIARRHPYFY
HHHH H HHHHHHHH HHHHHHHH HHHH

IV
151 APELLFFAKR YKAAFTECCO AADKAACLLP KLDEL RDEGK ASSAKQRLKC
HHHHHHHHHH HHHHHHHHH HHHHH HHHHHHHHH HHHHHHHHH

201 ASLQKFGERA FKA^VAVARLS QRFPKAEFAE VSKLVTDLT^VK VHTECC^VHGDL
 HHHHH HH HHHHHHHHHH HH HHH HHHHHHHHHH HHHHHH HH

VI VII

251 LECADDRADL AKYICENODS ISSKLKECCE KPLLEKSHCI AEVENDEMPA

HHHHHHHHHH HHHH HH HH HHHHHHH H

301 DLPSLAADFV ESKDVCKNYA EAKDVFLGMF LYEYARRHPD YSVVLLRLRLA
HHHH HHHHHH HHHHHH HHHHHH HHHHHHHH

VIII

351 KTYETTTLEKC CAADPHECY AKVFDEFKPL VEEPQNLIKQ NCELFEQLGE
 HHHHHHHHHH HH H HHHHH HHHHHHHHHH HHHHHHH

401 YKFQNALLVR YTKKVPQVST PTLVEVSRNL GKVGSKCCKH **PEAKRMP**CAE
 HHHHHHHHHH HHHH H HHHHHHHHHH HHH HHHHHHHH

451 DYLSVVLNQL CVLHEKTPVS DRVTKCCTES LVNRRPPCFSA LEVDETYVPK
 HHHHHHHHHHHH HHHHHH HHHHHHHHHH HHHHHHHH

501 EFNAETFTFH ADICTLSEKE RQIKKQTALV ELVKHKPKAT KEQLKAVMDD
HHH HHH HHHHMMEMHH HHH HHHHHHHH

XII

551 FAAFVEKCKK ADDKETCFAE EGKKLVAAASQ AALGL
HHHHHHHH HHHH HHHHHHHHHH HH

Loop

I	Val54-Asn61
II	Thr76-Asp89
III	Ala92-Glu100
IV	Gln170-Ala176
V	His247-Glu252
VI	Glu266-Glu277

Loop

VII	Glu280-His288
VIII	Ala362-Glu368
IX	Lys439-Pro447
X	Val462-Lys475
XI	Thr478-Pro486
XII	Lys560-Thr566

Figure 10

a. Randomisation of Loop IV.

IV
151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHH HHHHHHHHHH

IV
151 APELLFFAKR YKAAFTECCX XXXXXXXXCLLP KLDEL RDEGK ASSAKQRLKC
HHHHHHHHHH HHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

X represents the mutation of the natural amino acid to any other amino acid. One, more or all of the amino acids can be changed in this manner. This figure indicates all the residues have been changed.

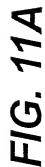
b. Insertion (or replacement) of Randomised sequence into Loop IV.

 $(X)_n$

↓

IV
151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDELRLDEGK ASSAKQRLKC
 HHHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

The insertion can be at any point on the loop and a length where n would typically be 6, 8, 12, 20 or 25.



TO FIG. 11B

TO FIG. 11B

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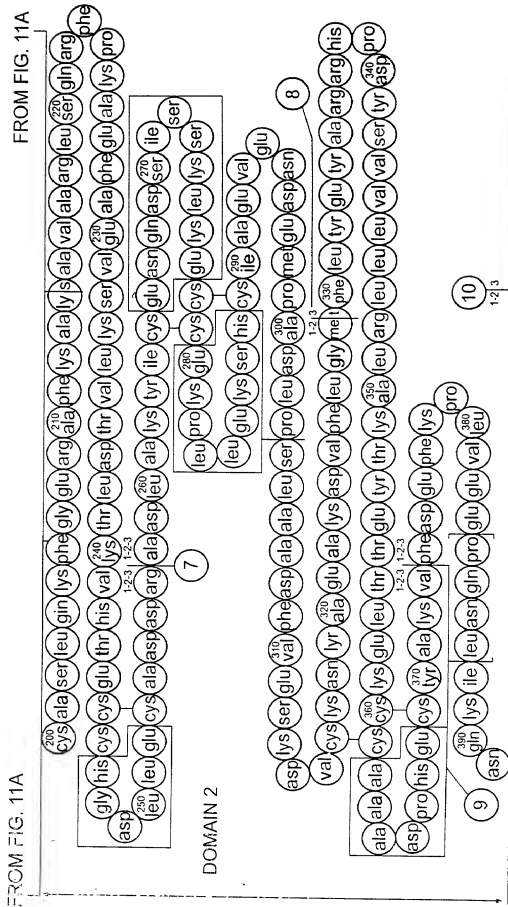


FIG. 11B

FOR THE RECORD

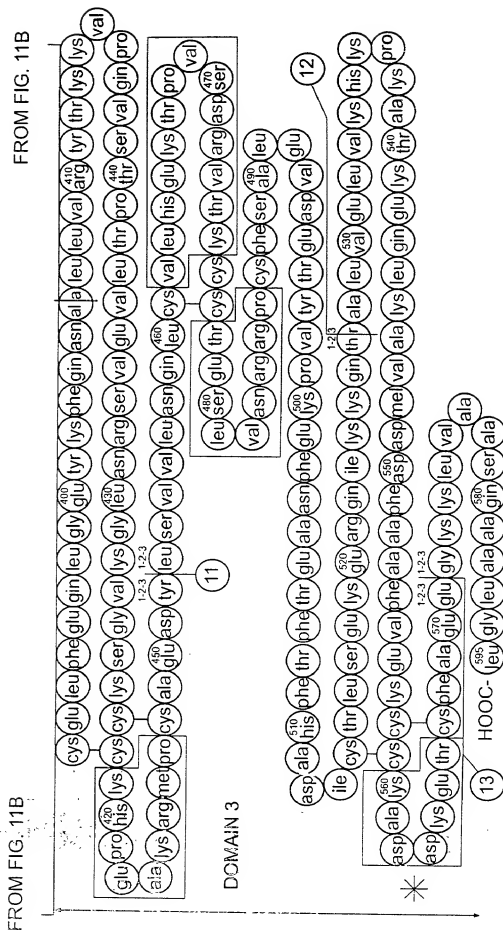


FIG. 11C

10/280* F11E860

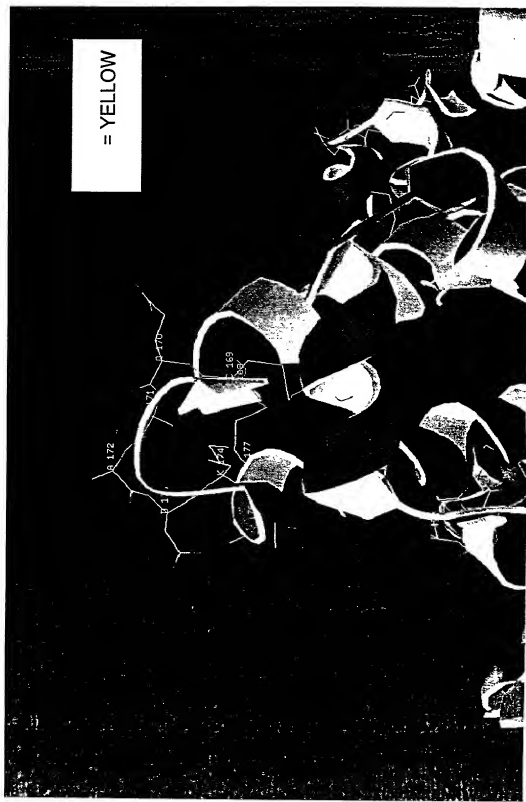


FIG. 12:
LOOP IV GLU170-A176

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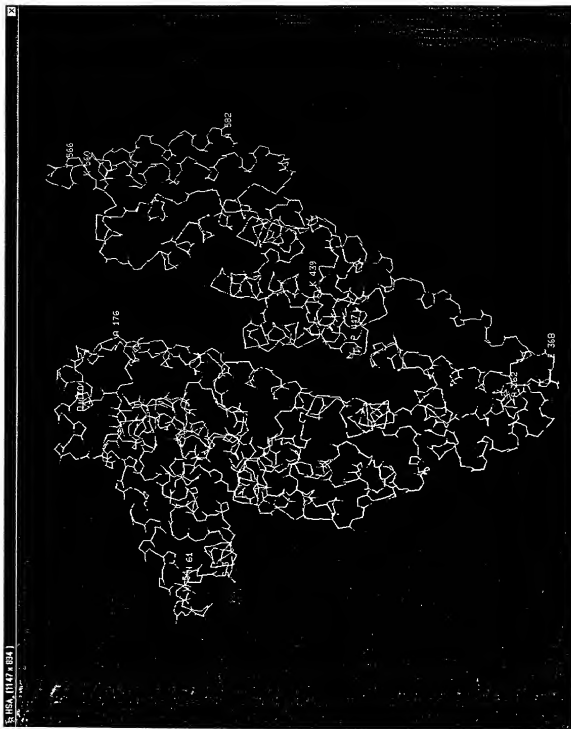


FIG. 13
TERTIARY STRUCTURE OF HA

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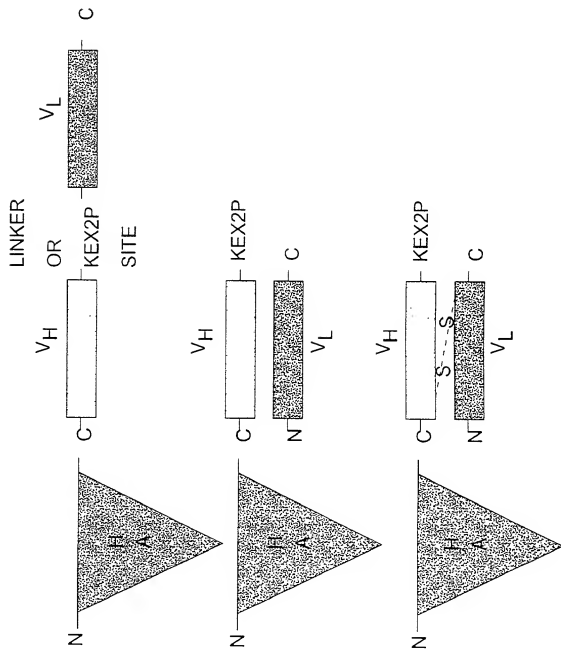


FIG. 14

10/28/2011 11:58:60

1 GAT GCA CAC AAG AGT GAG GTT GCT CAT CGG TTT AAA GAT TTG GGA GAA AAT TTC AAA 60
 1 D A H K S E V A H R F K D L G E E N F K 20

61 GCC TTG GTG ATT GCC TTT GCT CAG TAT CTT CAG CAG TGT CCA TTT GAA GAT CAT GAT 120
 21 A L V L I A F A Q Y L Q Q C P F E D H V 40

121 AAA TTA GTG AAT GAA GTA ACT GAA TTT CCA AAA ACA TGT GTT GCT GAT GAG TCA GCT GAA 180
 41 K L V N E V T E F A K T C V A D E S A E 60

181 AAT TGT GAC AAA TCA CTT CAT ACC CTT TTT GGA GAC AAA TTA TGC ACA GTT GCA ACT CTT 240
 61 N C D K S L H T L F G D K L C T V A T L 80

241 CGT GAA ACC TAT GGT GAA ATG GCT GAC TGC TGT GCA AAA CAA GAA CCT GAG AGA AAT GAA 300
 81 R E T Y G E M A D C C A K Q E P E R N E 100

301 TGC TTC TTG CAA CAC AAA GAT GAC AAC CCA AAC CTC CCC CGA TTG GTG AGA CCA GAG GTT 360
 101 C F L Q H K D D N P N L P R L V R P E V 120

361 GAT GTG ATG TGC ACT GCT TTT CAT GAC AAT GAA GAG ACA TTT TTG AAA AAA TAC TTA TAT 420
 121 D V M C T A F H D N E E T F L K K Y L Y 140

421 GAA ATT GCC AGA AGA CAT CCT TAC TTT TAT GCC CGG GAA CTC CTT TTC TTT GCT AAA AGG 480
 141 E I A R R H P Y F Y A P E L L F F A K R 160

Figure 15A

10/28/2011 11:22:28 AM

481 TAT AAA GCT GCT TTT ACA GAA TGT TGC CAA GCT GCT GAT AAA GCT TGC CTG TTG CCA 540
 161 Y K A A F T E C C Q A A D K A A C L L P 180

541 AAG CTC GAT GAA CTT CGG GAT GAA GGG AAG GCT TCG TCT GCC AAA CAG AGA CTC AAA TGT 600
 181 K L D E L R D E G K A S S A K Q R L K C 200

601 GCC AGT CTC CAA AAA TTT GGA GAA AGA GCT TTC AAA GCA TGG GCA GTG GCT CGC CTG AGC 660
 201 A S L Q K F G E R A F K A W A V A R L S 220

661 CAG AGA TTT CCC AAA GCT GAG TTT GCA GAA GTT TCC AAG TTA GTG ACA GAT CTT ACC AAA 720
 221 Q R F P K A E F A E V S K L V T D L T K 240

721 GTC CAC ACG GAA TGC TGC CAT GGA GAT CTG CTT GAA TGT GCT GAT GAC AGG GCG GAC CTT 780
 241 V H T E C C H G D L L E C A D D R A D L 260

781 GCC AAG TAT ATC TGT GAA AAT CAG GAT TCG ATC TCC AGT AAA CTG AAG GAA TGC TGT GAA 840
 261 A K Y I C E N Q D S I S S K L K E C C E 280

841 AAA CCT CTG TTG GAA AAA TCC CAC TGC ATT GCC GAA GTG GAA AAT GAT GAG ATG CCT GCT 900
 281 K P L L E K S H C I A E V E N D E M P A 300

901 GAC TTG CCT TCA TTA GCT GCT GAT TTT GTT GAA AGT AAG GAT GTT TGC AAA AAC TAT GCT 960
 301 D L P S L A A D F V E S K D V C K N Y A 320

Figure 15B

10/280*F11EE860

961 GAG GCA AAG GAT GTC TTC CTG GGC ATG TTT TTG TAT GAA TAT GCA AGA AGG CAT CCT GAT 1020
 321 E A K D V F L G M F L Y E Y A R H P D 340

1021 TAC TCT GTC CTG CTG CTG AGA CTT GCC AAG ACA TAT GAA ACC ACT CTA GAG AAG TGC 1080
 341 Y S V V L L L R L A K T Y E T T L E K C 360

1081 TGT GCC GCT GCA GAT CCT CAT GAA TGC TAT GCC AAA GTG TTC GAT GAA TTT AAA CCT CTT 1140
 361 C A A A D P H E C Y A K V F D E F K P L 380

1141 GTG GAA GAG CCT CAG AAT TTA ATC AAA CAA AAC TGT GAG CTT TTT GAG CAG CTT GGA GAG 1200
 381 V E E P Q N L I K Q N C E L F E Q L G E 400

1201 TAC AAA TTC CAG AAT GCG CTA TTA GTT CGT TAC ACC AAG AAA GTA CCC CAA GTG TCA ACT 1260
 401 Y K F Q N A L L V R Y T K K V P Q V S T 420

1261 CCA ACT CTT GTA GAG GTC TCA AGA AAC CTA GGA AAA GTG GGC AGC AAA TGT TGT AAA CAT 1320
 421 P T L V E V S R N L G K V G S K C C K H 440

1321 CCT GAA GCA AAA AGA ATG CCC TGT GCA GAA GAC TAT CTA TCC GTG GTC AAC CAG TTA 1380
 441 P E A K R M P C A E D Y L S V V L N Q L 460

1381 TGT GTG TTG CAT GAG AAA ACG CCA GTA AGT GAC AGA GTC ACA AAA TGC TGC ACA GAG TCC 1440
 461 C V L H E K T P V S D R V T K C C T E S 480

Figure 15C

10/280-11122860

1441 TTG GTG AAC AGG CGA CCA TGC TTT TCA GCT CTG GAA GTC GAT GAA ACA TAC GTT CCC AAA 1500
 481 L V N R R P C F S A L E V D E T Y V P K 500

1501 GAG TTT AAT GCT GAA ACA TTC AOC TTC CAT GCA GAT ATA TGC ACA CTT TCT GAG AAG GAG 1560
 501 E F N A E T F T F H A D I C T L S E K E 520

1561 AGA CAA ATC AAG AAA CAA ACT GCA CTT GTT GAG CTT GTG AAA CAC AAG CCC AAG GCA ACA 1620
 521 R Q I K K Q T A L V E L V K H K P K A T 540

1621 AAA GAG CAA CTG AAA GCT GTT ATG GAT GAT TTC GCA GCT TTT GTA GAG AAG TGC TGC AAG 1680
 541 K E Q L K A V M D D F A A F V E K C C K 560

1681 GCT GAC GAT AAG GAG ACC TGC TTT GCC GAG GAG GGT AAA AAA CTT GTT GCT GCA AGT CAA 1740
 561 A D D K E T C F A E E G K K L V A A S Q 580

1741 GCT GCC TTA GGC TTA TAA CAT CTA CAT TTA AAA GCA TCT CAG 1782
 581 A A L G L * 585

Figure 15D